

TREATMENT OF SYPHILIS WITH SILVER-SALVARSAN *

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This is a preliminary report based upon over two hundred intravenous injections of silver-salvarsan.

Syphilologists are familiar with the history and the chemical composition of the silver-salvarsan. It will, therefore, be sufficient to state the following facts:

Kolle, who succeeded Ehrlich, succeeded also in the production of silver-salvarsan, which has the advantage over neo-salvarsan of being very stable, easily soluble, and considerably less toxic. In a 20 per cent solution it is isotonic. Silver-salvarsan is even less toxic than some sodium preparations that were elaborated after neo-salvarsan.

Colloidal silver by itself has been shown to have more spirochaetecidal influence than mercury

Though German authorities have published excellent results in the treatment, mainly of neurosyphilis, and while we knew something of the influence of silver upon nerve lesions, we started the use of this new drug silver-salvarsan hesitatingly, very carefully using careful technic. We invariably started with an initial dose of 0.1 gm., and then increased to 0.2 gm., and finally to the maximal dose of 0.3 gm. From eight to twelve injections were given.

The solution is dark-brown, and patients who had salvarsan or neo-salvarsan before were told so beforehand.

We saw no untoward reaction of any kind in any of the patients. One patient who, after each of three injections of neo-salvarsan, showed very pronounced and very disagreeable general and cutaneous reactions, tolerated one small dose of silver-salvarsan very well.

Our results were uniformly good. Early syphilitic manifestations disappeared rapidly. One patient whose Wassermann reaction had remained positive in spite of two years' intensive anti-syphilitic treatment, showed a negative reaction six weeks after twelve injections of silver-salvarsan. Another patient, with a somewhat mysterious and disfiguring facial syphilis, and who was previously treated in every possible way with slow but rather insignificant results, is rapidly improving and being made happy.

Silver-salvarsan injections may be combined with other treatments, without any danger. We use intravenous injections of cyanide of mercury on the days when no silver-salvarsan is given, and give the silver-salvarsan at intervals of from three to five, and even eight days.

We consider silver-salvarsan to be a very valuable addition to the armamentarium against syphilis.

THE EARLY DIAGNOSIS AND THE TREATMENT OF CANCER OF THE CERVIX *

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If any apology is needed for a paper on the subject of "Cancer of the Cervix," that apology is

found in the fact that the ultimate mortality rate is very close to 100 per cent, and the additional fact that this disgraceful rate is due in large part to late diagnosis.

The absolute necessity for an early diagnosis, if a cure is to be within the realm of possibility, rests upon anatomical, and the possibility of cure through early operation upon pathological grounds.

Anatomically, even the least perceptible extension of the growth beyond the cervix in any direction means that bladder, rectum or ureters are involved, while if the growth is confined to the cervix without direct extension through tissue involvement, glandular metastases are relatively late or do not occur at all; therefore the prognosis following early diagnosis and removal should compare favorably with the prognosis following early operation for cancer of the breast, in which early tissue involvement by direct extension of cancer cells to organs not amenable to operative treatment is less to be feared than early glandular metastasis.

The reasons an early diagnosis is rarely made are many, and not all of them by any means are attributable to carelessness on the part of the general practitioner, as is too frequently assumed. On the contrary, much of the responsibility for this must be shared by the lay tradition that more or less menstrual disturbance in the form of menorrhagia or metrorrhagia is normal at the menopause, to the familiarity of every woman with the periodical hemorrhage of menstrual life, and to the ancient belief that cancer means pain, foul discharge, and cachexia.

This periodical discharge of blood from the genital tract and the leucorrhea which sometimes follows trifling indiscretion leads the patient to ignore irregular menstrual frequency and leucorrhea as she approaches the menopause, and by reason of the tradition above mentioned she refuses to become excited over a slight increase in the menstrual flow or shortening of the inter-menstrual interval.

One of the most damnable symptomatic triads that ever occupied either the professional or lay mind is that pain, foul discharge, and cachexia, are requisite before a diagnosis can be made or the suspicion aroused that cancer may be present. Whereas, the truth is that pain means positive extension beyond the confines of the cervix, foul discharge that saprophytic infection of dead or dying tissue has occurred, and cachexia that hopeless toxic absorption is taking place.

In tracing back the onset of the two really early symptoms, viz., watery leucorrheal discharge and inter-menstrual spotting, one is surprised to learn how often this onset synchronized with the patient's highest state of nutrition as evidenced by her having at that time reached her maximum weight and sense of well-being. This alone is sufficient to lull the most intelligent woman into a belief that nothing serious can be wrong with her.

For these ideas of the laity, the profession as a whole is at fault insofar as it has failed to educate

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that portion of the public which is willing to be educated and will listen to professional advice; as to all others the responsibility is theirs and theirs alone. Bearing only directly upon the subject proper, is it not true that the profession itself would stand upon a higher plane in public estimation today if it bent more of its efforts in the direction of public education upon medical topics, taught its individual patients more of the aims and altruistic motives of the profession, and then resigned its Don Quixotic battles with the windmills of the fakes to the public, since, after all, it is the health and life of the community as a whole that is at stake, not the welfare of doctors in the community?

It is perfectly well realized that public education alone would fall far short of solving the entire problem of early diagnosis of cancer of the cervix, even if that were carried to the extreme of frequent examinations at or about the time of the menopause; first, because it would leave outside the pale those instances of rapidly growing carcinoma which occur in young women, and second, because of the diagnostic difficulties often encountered in early cases unless the examiner is thoroughly impressed with the idea that a sufficiently early diagnosis can be made with the microscope, *and only with the microscope*. I know that this statement will be questioned by some, and it may well be that my diagnostic acumen is not equal to the best, but the opinion is honest and is based upon thirty years of experience, with a by no means enormous but not unreasonably limited clientele. If we look our failures as squarely in the face as our successes and trace our cases to their ultimate outcome I am satisfied there will be little dissent from the opinion that a positive clinical diagnosis of cancer means a cancer death sooner or later, while a diagnosis so early that it must be made by the pathologist gives a high percentage of cures.

The physical signs in the curable stage are thoroughly deceptive. Inspection may reveal nothing wrong with the early cancerous cervix that is not equally apparent in the cervix of any multipara who has sustained a laceration with chronic infection and erosion, or there may be a few pinpoint yellowish spots underneath the mucosa so insignificant in size as to be overlooked. Neither may there be anything on palpation to arouse the suspicion of an examiner accustomed to palpating Nabothian follicles in the cervix of practically every woman who has borne children, that is nothing unless it may be the withdrawal of a blood-stained finger at the close of the examination.

Supposing, however, that, as opportunity offered, the family physician informed every parous woman in his clientele that any menstrual change at the menopause excepting diminution of the flow was abnormal, that profuse menstruation, intermenstrual spotting, or recent leucorrhea demanded investigation to determine its origin, and supposing further that when this investigation was made if the cervix were not absolutely normal or the con-

dition not plainly explained by a mucous polyp a section were removed and submitted to a competent pathologist, would not many cases still in the curable stage be discovered that now are condemned to a slow, painful death by one of the most horrible routes?

If, in addition to this increased activity on the part of the general practitioner, the surgeon *routinely* submitted to the pathologist all specimens from cervixes he felt called upon to repair or amputate for infection, laceration, or hypertrophy, deaths from cancer of the cervix would tend to be confined to those groups who profess to believe that the manifestations of disease are immaterial things which can be corrected through vicarious appeals to an immaterial Almighty who will lend an ear, however, only if these are backed up by so much very material lucre per appeal, and to those who are fond of having their necks twisted and legs pulled simultaneously.

Once more, allow me to diverge from the subject proper to call attention to the fact that the permanent survival of the science and art of medicine depends upon the constant, continuous, day by day demonstration that scientific medicine secures definite, tangible results which pseudo-science does not and can not accomplish.

It will be seen that I am neither advising startling diagnostic methods, nor putting forth any new procedures. On the contrary it is felt that if the well known time-tried methods were used systematically and pushed to the uttermost limits of their usefulness the apparition of the anæmic hopeless cancer case, which every surgeon dreads, would be less frequently observed, and the border line cases which he sees from day to day, in which hope alternates with dread only to give way to despair as time reveals the uselessness of accepted measures would be throttled at their onset, with what mitigation of human suffering and prolongation of life one hardly dares conjecture.

TREATMENT

Again I recognize that we are treading on debatable ground, but one can do no better than record his personal opinion and observed results. Bald statistics are not presented; first, because my own are not available, my case records not having followed me as yet; second, because statistics that do not run into the thousands are almost worthless; and third, because statistics presented without all possible collateral data can be made to prove almost anything an essayist wishes.

First, as to prophylaxis, and in this I wish to make myself perfectly clear. I am emphatically opposed to unnecessary operations on the cervix and uterus. Curretage, other than diagnostic, is a rarity, and repair of cervical laceration in a woman well within the child-bearing age is never performed unless that laceration is the site of an infection which is making her miserable by reason of discharge or broad ligament lymphangitis and cellulitis. Further, I believe that the orgy of therapeutic currettings, trachelorrhaphies, and oophorectomies which swept over the profession with the advent of aseptic surgery, was a dis-

grace, so that I cannot possibly be misunderstood in the assertion of my opinion that the first active step in the prophylaxis of cancer of the cervix is the amputation of every cervix in parous women *beyond the child-bearing age* in which there is an unhealed laceration, marked erosion and hypertrophy; and cancer of the cervix in nulliparæ is negligible.

As stated before, submission of the removed material to the pathologist should be a routine procedure, and in this class are found almost all of my own complete successes following the radical operation, together with a few others in whom some symptom had aroused a suspicion which could not be verified or refuted clinically, but in which the diagnosis was made by the pathologist from specimens removed from the cervix for that purpose. In other words, the successful cases were almost all in the class in which the diagnosis was made accidentally as it were.

Further, so far as I know, all of these are living: per contra—with an occasional startling exception—all of those operated upon by *any method* more than five years ago are dead or have had a recurrence if the operation were based upon a readily made clinical diagnosis.

The radical operation above referred to was, in most instances, a combined vaginal and abdominal operation, the cervix being sterilized at the time of, not before, the operation with the thermocautery, the cervical canal then closed by suturing and the incision through the vaginal mucosa made with the cautery.

The broad ligament removal was made either mediad or lateral to the ureters as the circumstances of the individual case seemed to dictate. Two or three were vaginal hysterectomies, the vaginal incision being made with the cautery and the broad ligaments clamped, not tied, so that the destruction of tissue extended beyond the line of broad ligament sectioning. One case, still well after five years, had only a high amputation with the cautery followed after complete healing by radium treatments. In this case the cautery amputation was not on the heat principle first enunciated by Doyen and so elaborately and well worked out by Percy, but followed the lines of high amputation as advocated by John Byrne many years ago.

If I had the absolute courage of my convictions I should advocate the treatment of all *pathologically* but not *clinically* diagnosable cases of cancer of the cervix by high cautery amputation followed by the use of radium. Not having yet arrived at that stage, and in view of the opinions of operators of much greater experience, I still hesitate to take so radical a step and therefore continue to advocate the radical operation for cases in their very early stage—but I think we are coming to the former nevertheless.

Taking now the other extreme, the cases frankly unsuitable for any type of radical operation, those having profuse foul discharge and bleeding, with definite fixation of the uterus and

deep excavation, or with cauliflower excrescences filling the vaginal vault.

Having run the entire gamut of curette and cautery in the early days, zinc chloride cauterization and acetone later, being misled by exuberant enthusiasm into radical operation as a last resort in a few instances, utilizing the Percy method to the limit in others, and finally turning to radium on the basis of "any port in a storm," I am thankful to have found a legitimate reason to drop all operative procedures and depend upon radium as the sole *palliative* measure which squares with my surgical conscience.

There is more than one reason for this attitude. Primarily, it is because without the pain of operation or discomfort of anæsthesia patients have experienced more relief from this than from any other method. Secondly, because every unsuccessful painful operation is an opprobrium to the profession and a deterrent to the prompt seeking of relief by others.

Coming now to the great class of border line cases, which no hard and fast rule can govern and in which each individual patient must be studied as a unit, not as a member of a class, many factors that deserve consideration must be passed over for lack of time. One that may be discussed, however, is free mobility of the uterus or its fixation as the important feature in deciding for or against a radical operation. If my previous contention is true that any extension beyond the cervix means that the case is probably hopeless so far as radical operation is concerned it follows that fixation is an absolute bar to any radical procedure. However, nearly every authority makes the statement that fixation may be due to inflammatory infiltration and therefore not be a bar to radical removal. Theoretically this may be true, but practically we know that every case has more widespread pelvic involvement once the abdomen is opened than was thought possible when the examination was made.

The age of the patient, the condition of her kidneys, heart and lungs, and above everything, her expressed desire after the condition and prognosis have been fully explained, must be taken into account before deciding whether any operation is justifiable, and if so, which is preferable. One may get away successfully with a pan or vaginal hysterectomy with the cautery in one instance, with the elaborate Percy procedure in another, with high cautery amputation followed by radium in another, or with radium followed by any of these procedures in still another, but the successes are in pitiable contrast to the failures.

Being one of those surgeons who believe that every mutilating operation is a confession rather than a subject for boasting, and that when equally good results follow no operation and no mutilation, it is an evidence of professional progress not to operate, the writer would like to summarize the foregoing with the double object of promoting discussion and standardizing our procedures so far as our present knowledge permits.

1. A pre-clinical, microscopic, diagnosis of

cancer of the cervix is necessary if there is to be a tangible hope of permanent cure from any of the surgical procedures with which we are familiar.

2. Early diagnosis can be attained through the education of the individual patient by her personal physician, by removal of a section for examination from every cervix in the least suspicious, and by the routine pathological examination of specimens from every case in which repair or amputation has been performed.

3. Many cases of cancer of the cervix might be prevented if high amputation were adopted as a routine procedure in every case of lacerated eroded hypertrophied cervix found in women beyond the probable child-bearing age.

4. As a rule, with but few exceptions, radical pan-hysterectomy should be limited to those cases which are discovered before any marked symptoms or positive physical signs are present.

5. In the general interests of humanity and humaneness, all bloody or painful procedures should be abandoned in late cases, and palliation by radium adopted as the routine procedure.

6. In border line cases the condition and outlook should be presented with the utmost frankness and the patient's desires should then have as much weight as any other factor in determining how the case should be managed.

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NOTICE

The December Journal will contain a symposium on Industrial Medicine.

THE VALUE OF BLOOD STUDIES*

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Modern methods of bio-chemistry and physiology have introduced a new conception of the value of blood studies, not only in the understanding of anæmias, either primary or secondary, but also in the study of many other diseases. A true value of the function of kidneys can be better appreciated through a study of the blood than by a study of the urine. In the same way some of the newer methods of analyzing the blood throw light on diseased conditions in other organs, such as the liver, and lungs, and in the complicated problems connected with digestion.

Hemoglobin may be present in sufficient volume and yet the oxygen be unable to be carried or given off in sufficient amounts to satisfy the needs of the tissue cells throughout the body. An example of the inability of the red blood cells to give off oxygen, even though the hemoglobin is present in normal amounts, is that produced by simple cold. Another example is the presence of abnormal salt concentration of the plasma. Exactly how these two factors of temperature and salt contents of the plasma affect the affinity of hemoglobin for oxygen is not well known. The amount of oxygen that can be taken up, and the rapidity with which oxygen can be given off, varies with the temperature of the body. This is

an important factor in the temperature regulation during early infancy. All who have watched newborn infants with disturbed temperature regulations have noted the cyanosis which occurs in these infants with a low body temperature.

The fact that hemoglobin is a colloid and the knowledge we have of the interrelation of electrolytes and colloids makes it evident that the salt content of the blood must affect and regulate to a certain extent the transfer of oxygen. It has been shown that potassium salts are capable of causing hemoglobin to absorb oxygen to some degree. Many studies have demonstrated the fact that the loss of water with the resulting concentration of salts affects the oxidation of the tissues. The buffer quality of these salts undoubtedly affects the oxygen transfer from the hemoglobin to the body cells. This is, as we know, intimately connected with another factor, the hydrogen ion concentration of the blood. It is well known that increasing the acidity of the blood lessens its active concentration of oxygen. The importance of studying the relation of hemoglobin to the three factors, temperature, electrolytes and hydrogen ion concentration, is indicated in the study of almost all blood diseases.

The morphological study of blood furnishes very reliable data as to the condition of the blood-forming organs. Normally the blood level is kept up by daily destruction and replacement of cells. Ashby has recently determined, by estimating the disappearance of cells transfused by the differential agglutination test, that the normal life of the red blood cell is approximately thirty days.

Destruction is continually carried on by the following processes:

FIRST. By phagocytosis. The endothelial cells of the spleen, liver and other organs take part in this process.

SECOND. By fragmentation. This is shown by the occurrence of microcytes and poikilocytes. Fragmentation is produced in the circulation and not in the bone marrow. Normally, there are a few such cells always present within the circulation, but under pathological conditions, when young cells are thrown out in large numbers, these young cells cannot stand the functional strain put on them and become easily fragmented. Under pathological conditions, not only fragmenting cells, but also cells with vacuoles may be found. These ultimately become hemoglobin dust and are removed from the circulation to be stored in the spleen. Such hemoglobin dust is found normally in the spleen, but appears in much greater quantity in anemic conditions.

THIRD. Destruction occurs by hemolysis. Under normal conditions this probably plays very little part, as hemolysis is normally an intra-cellular process, but in pathological conditions it may play a big part. Under such conditions hemoglobinuria occurs often accompanied by fever and chills.

FOURTH. Disintegration is also shown by the increased fragility of the red blood cells. This is especially found in certain pathological conditions, such as congenital hemolytic icterus, in which there is pronounced blood destruction.

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